

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Passive smoking at home is a risk factor for community-acquired pneumonia in older adults: a population-based case-control study
AUTHORS	Almirall, Jordi; Serra-Prat, Mateu; Bolibar, Ignasi; Palomera, Elisabet; Roig, Jordi; Hospital, Imma; Carandell, Eugenia; Agustí, Mercè; Ayuso, Pilar; Estela, Andreu; Torres, Antoni

VERSION 1 – REVIEW

REVIEWER	Giovanni Viegi, MD CNR Institutes of Clinical Physiology and Biomedicine and Molecular Immunology, Pisa and Palermo (Italy)
REVIEW RETURNED	07-Apr-2014

GENERAL COMMENTS	<p>The issue is of current interest. The study design and population are adequate. There is some additional limitation in exposure assessment and data integration which are reported in the comments for the Authors.</p> <p>Page 2, "Key messages", "Passive smoking at home might be a risk a factor...": is or is not? Sentence is to be changed according to comments to the text.</p> <p>Page 3, "Abstract" - line 8: change in "...CAP was estimated in 1.14 cases x 10⁻³ inhabitants in..." - line 16: "Passive smoking at home is a risk factor..." instead of "Passive smoking at home might e a risk factor..." "Strenghts and limitations of the study": to add, as limit, the imprecision of the exposure question</p> <p>Page 4, "Introduction" - First two sentences: old references, please, update. With special mention to epidemiological studies in Mediterranean countries (e.g. Italy) which have a comparable climate to Spain. In addition, two recent reviews have been published and are relevant herein (Torres A, et Thorax 2013; Torres A, et al Eur J Clin Microbiol Infect Dis 2014).</p> <p>Page 6, "Patients and methods", lines 3-4, question "Do you currently live with one or more smokers at home?": this question is not directly related to exposure. Co-inhabitants who smoke may go to smoke outside.</p> <p>Page 7, "Data analysis", sentence "Regarding the case-control...": this is unclear in view of the control sampling procedure described at page 5 and casts some doubts on the generalizability of the results from the case-control study.</p>
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	<p>Page 7, "Results"</p> <ul style="list-style-type: none"> - sentence "...reported to be in contact with tobacco smoke at home...": this terminology is imprecise; see comment for page 6, "Patients and methods", lines 3-4 - line 3 from bottom: "...was not associated with other known..." instead of "...was not associated with other known..." <p>Page 8, "Discussion", sentence "...in adults general population passive exposure to tobacco smoke at home is not a risk factor for CAP, ...": this is an inadequate terminology. In the overall population there is an excess of risk and incidence, although it does not reach the conventional level of significance for the risk. In explanatory epidemiological studies, it is preferable to get the chance of doing a type I error rather than type II error. This comment here is more relevant in view of the imprecision of the exposure question.</p> <p>Page 9, "Discussion", sentences "Age seems to modify....provoked by other smokers": the Discussion herein is incomplete. The Authors, in view of the imprecision of their exposure assessment, should cite the possibility that either the length of exposure or the exposure pattern may have relevance. Indeed, it is possible that younger partners of passive smoking exposed subjects' go to smoke outside the house, whereas older partners do not.</p> <p>Page 10, "Discussion"</p> <ul style="list-style-type: none"> - line 2: "...age who cannot quit to be exposed to passive smoking..." instead of "...age exposed to passive smoking..." - line 3, "In summary... is controversial": ??; see comment for page 8 "Discussion" - last line: "...such as changes in life style factors or vaccination" instead of "... such as vaccination or changes in life style factors"
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REVIEWER	Charles Feldman University of the Witwatersrand South Africa
REVIEW RETURNED	15-Apr-2014

GENERAL COMMENTS	<p>There is no mention in the current study about whether the authors had ethics approval and whether patients consented. It may well be in the initial publication, but needs to be repeated in the current paper.</p> <p>This was a population-based case-control study designed to assess risk factors for CAP, and the current manuscript details the findings related to home exposure to passive smoking. The main positive finding was that passive smoking at home might be a risk factor in older adults > 65years.</p> <p>COMMENTS</p> <ol style="list-style-type: none"> 1) The authors did not assess other passive smoke exposures in the patients, such as in the workplace or in the community (e.g. public places). Could these exposures have influenced the results? Alternatively is there legislation in place in Spain to comprehensively protect workers against work-place exposure? Perhaps this could be discussed briefly and if it is a potential limitation, included as such in the discussion. 2) If workplace exposure is a possibility, was there any difference in those that were or were not working? 3) Much of the second half of the results section in the abstract is
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	<p>not included in the results section in the main body of the text and it should be</p> <p>4) It would be interesting for the readers to know the median age and the age range of the patients/controls</p> <p>5) The difference in annual incidence of CAP comparing those exposed and those not exposed in the overall study population does look to be significant (RR 1.26; 95% CI 1.02-1.55)</p> <p>6) Was the fact that the major difference was found in those > 65 years not possibly due to a longer passive exposure time rather than any modification caused by age itself?</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

1. Page 2, "Key messages", "Passive smoking at home might be a risk a factor...": is or is not? Sentence is to be changed according to comments to the text.

The sentence has been changed.

2. Page 3, "Abstract"

- line 8: change in "...CAP was estimated in 1.14 cases x 10⁻³ inhabitants in..."

Changed.

- line 16: "Passive smoking at home is a risk factor..." instead of "Passive smoking at home might e a risk factor..."

Changed.

- "Strenghts and limitations of the study": to add, as limit, the imprecision of the exposure question

Added.

3. Page 4, "Introduction"

- First two sentences: old references, please, update. With special mention to epidemiological studies in Mediterranean countries (e.g. Italy) which have a comparable climate to Spain. In addition, two recent reviews have been published and are relevant herein (Torres A, et Thorax 2013; Torres A, et al Eur J Clin Microbiol Infect Dis 2014).

The first two references have been changed for more recent one from Torres et al. (2013-2014).

4. Page 6, "Patients and methods", lines 3-4, question "Do you currently live with one or more smokers at home?": this question is not directly related to exposure. Co-inhabitants who smoke may go to smoke outside.

The English translation of this question perhaps is not accurate enough. The Spanish version refers clearly to "live together with one or more smokers at home" which is easily interpreted as being exposed to tobacco smoke at home. We agree that this measure may be quantitatively inaccurate

but, in any case, we believe that it is a reasonable and useful indicator of passive exposure to tobacco at home. Moreover, the Spanish law does not allow smoking in indoor public places so that passive exposure to tobacco smoke can only occur at home or private houses. This exposure is the objective of our study.

5. Page 7, "Data analysis", sentence "Regarding the case-control...": this is unclear in view of the control sampling procedure described at page 5 and casts some doubts on the generalizability of the results from the case-control study.

A large case-control study was performed in which cases were "frequency matched" by age and sex with controls. However, for the purposes of the present analysis only never smokers were selected from the overall sample. When selecting this subgroup of subjects, age and sex homogeneity between cases and controls may be altered, so the effect of passive tobacco was adjusted by these two variables. We believe that this question is clearly described in the methods section.

6. Page 7, "Results"

- sentence "...reported to be in contact with tobacco smoke at home...": this terminology is imprecise; see comment for page 6, "Patients and methods", lines 3-4.

Idem as in point 4.

- line 3 from bottom: "...was not associated with other known..." instead of "...was not associated with other known..."

Changed.

7. Page 8, "Discussion", sentence "...in adults general population passive exposure to tobacco smoke at home is not a risk factor for CAP, ...": this is an inadequate terminology. In the overall population there is an excess of risk and incidence, although it does not reach the conventional level of significance for the risk. In explanatory epidemiological studies, it is preferable to get the chance of doing a type I error rather than type II error. This comment here is more relevant in view of the imprecision of the exposure question.

According to the reviewer suggestion we have modified this sentence in the discussion. We would like to remark that the stratified analysis by age groups shows a clear interaction or effect modification of age group, since passive smoking showed a positive and significant effect in >65 year and showed no effect in <65 years. However, we do not know if this interaction is due to the age "per se" or to an age-related exposure accumulation.

8. Page 9, "Discussion", sentences "Age seems to modify....provoked by other smokers": the Discussion herein is incomplete. The Authors, in view of the imprecision of their exposure assessment, should cite the possibility that either the length of exposure or the exposure pattern may have relevance. Indeed, it is possible that younger partners of passive smoking exposed subjects' go to smoke outside the house, whereas older partners do not.

We have added a sentence in the discussion section in relation to the length and pattern of exposure to passive tobacco smoke.

9. Page 10, "Discussion"

- line 2: "...age who cannot quit to be exposed to passive smoking..." instead of "...age exposed to passive smoking..."

Changed

- line 3, "In summary... is controversial": ??; see comment for page 8 "Discussion"

Changed. See answer to point 7 and 8.

- last line: "...such as changes in life style factors or vaccination" instead of "... such as vaccination or changes in life style factors"

Changed.

Reviewer: 2

There is no mention in the current study about whether the authors had ethics approval and whether patients consented. It may well be in the initial publication, but needs to be repeated in the current paper.

Ethical approval statement is included on page 6 (methodology section).

1) The authors did not assess other passive smoke exposures in the patients, such as in the workplace or in the community (e.g. public places). Could these exposures have influenced the results? Alternatively is there legislation in place in Spain to comprehensively protect workers against work-place exposure? Perhaps this could be discussed briefly and if it is a potential limitation, included as such in the discussion.

As the reviewer suggest we have added a study limitations paragraph referring to the imprecision of the exposure measure and to passive exposure at work.

2) If workplace exposure is a possibility, was there any difference in those that were or were not working?

If subjects are not working they cannot be exposed at workplace.

3) Much of the second half of the results section in the abstract is not included in the results section in the main body of the text and it should be.

These results are included in Table 1. We believe that it is not necessary to duplicate information (in the text and in the table).

4) It would be interesting for the readers to know the median age and the age range of the patients/controls.

Median and range of age have been introduced.

5) The difference in annual incidence of CAP comparing those exposed and those not exposed in the overall study population does look to be significant (RR 1.26; 95% CI 1.02-1.55)

Yes, the reviewer's comment is correct but the stratified analysis showed a clear interaction with age.

6) Was the fact that the major difference was found in those > 65 years not possibly due to a longer passive exposure time rather than any modification caused by age itself?

This is a possibility and an interpretation of the results that has been introduced in the discussion.